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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/393,302	09/10/99	HOVANESSIAN	A 03495.0166-0

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1645	15

DATE MAILED: 07/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/393,302	Hovanessian et al.
Examiner	**Art Unit**
Robert A. Zeman	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Sep 10, 1999*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above, claim(s) *1, 7, 8, 11, 12, and 14-21* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *2-6, 9, 10, and 13* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-23* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Election/Restriction

Applicant's election with traverse of Group II, as drawn to inhibitors comprising p95/nucleolin, in Paper No. 14 is acknowledged. The traversal is on the ground(s) that the restriction was improper since the Examiner did not demonstrate that examining all the claims together would be a serious burden but merely demonstrated that the inventions were independent and distinct. This is not found persuasive because searches of the claimed inventions would not be coextensive in scope.

The requirement is still deemed proper and is therefore made FINAL.

The amendment filed on 4-5-2001 is acknowledged. Claims 4-9, 14, 16-18 and 23 have been amended. Claims 1-23 are pending. Claims 1, 7-8, 11-12 and 14-23 have been removed from consideration. Claims 2-6, 9-10 and 13 are currently under examination.

Specification

The disclosure is objected to because of the following informalities: The Brief Description of Drawings (page 64) should be labeled as such instead of using the title "Figures".

Additionally, some of the Figures (Figure 49, for example) contain sequences. Said sequences must be identified by a SEQ ID NO. Please see 37 C.F.R. 1.821(d).

Appropriate correction is required.

Claim Objections

Claims 5-6, 9-10 and 13 objected to because of the following informalities: said claims contain an obvious typographical error. The term "anyone" should read "any one".

Claims 2-6, 9-10 and 13 are dependent on non-elected inventions.

Claims 4 and 9 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claims 6, 9, 10 and 13 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-6, 9-10 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is rendered vague and indefinite by the use of the phrase "peptidic or non-peptidic inhibitor molecule". It is unclear to what Applicant is referring. How does "peptidic and non-peptidic" refer to what is inhibited by the claimed molecule or a description of some feature that the claimed molecule possesses? How does "peptidic" differ from "non-peptidic"? As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim 2 is rendered vague and indefinite by the use of the phrase "**modify the interaction** between, **on the one hand** the V3 loop receptor according to claim 1 present on **the cell surface of a patient** infected with a **human HIV retrovirus,** specifically HIV-1 or HIV-2, and **on the other hand** the gp120 envelope protein of said HIV retrovirus".

- It is unclear what is meant by "modify the interaction". What interaction is being modified? How is said interaction modified? Is it enhanced? Inhibited?
- It is unclear what is meant by "on the one hand" and "on the other hand". Does the interaction take physically take place on the hands of a patient?
- It is unclear what is meant by "the cell surface of a patient". Does Applicant mean that said receptor appears on the exterior of an HIV infected patient or that a patient's cells have said receptor on their surfaces. If it is the latter, what cell types is applicant referring to? Is said receptor expressed by all cells or only selected cell types?
- The term human HIV retrovirus is redundant. HIV stands for human immunodeficiency virus. There are no non-human HIV viruses. Additionally, all HIVs are retroviruses.

- It is unclear whether HIV-1 or HIV-2 are meant to be limitations of the claims. Is "specifically" intended to be a suggestion or to introduce a Markush group?

For the reasons outlined above, it is impossible to determine the metes and bounds of the claimed invention.

Claim 3 is rendered vague and indefinite by the use of the term "peptide fragment". It is unclear what is meant by said term. How does a peptide fragment differ from a protein fragment? At what point does a "peptide fragment" become a "protein fragment"?

Claim 3 is rendered vague and indefinite by the use of the term "pseudopeptide counterpart". What is a pseudopeptide and how does it differ from a peptide? What is said "pseudopeptide" a counterpart to?

Claim 3 recites improper Markush language. It is unclear whether "pseudopeptide counterpart" is meant to be part of the Markush group.

Claim 4 is rendered vague and indefinite by the use of the phrase "which consists in a peptide or pseudopeptide". Is the claimed inhibitor part of a larger "peptide or pseudopeptide"? As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim 4 is rendered vague and indefinite by the use of the phrase "pseudopeptide which is homologous". What is a pseudopeptide? How does it differ from a "pseudopeptide counterpart"? What is said "pseudopeptide" homologous to? In what sense is it homologous? As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim 4 is rendered vague and indefinite by the use of the phrase " amino acid additions, deletions and or substitutions in the amino acid sequence of the inhibitor molecules according to claim 3". It is unclear what Applicant is referring to since claim 3 does not describe alterations of an amino acid sequence.

Claim 5 is rendered vague and indefinite by the use of the phrase "peptide bond is modified and replaced". Is said bond modified or replaced? If it is replaced why is it modified beforehand?. Additionally, which peptide bond is replaced? Does the claimed inhibitor contain only one peptide bond?

Claim 5 recites improper Markush language. The conjunction "or also" is improper. The final member of the Markush group should be preceded by "or".

Claim 6 is rendered vague and indefinite by the use of the phrase "chosen among". It is suggested that the phrase "selected from " or be used instead.

Claim 6 recites improper Markush language. The listing of group members should be preceded by "selected from" or "selected from the group consisting of" and the final member of the Markush group should be preceded by an "or" or an "and", respectively.

Claim 6 and 9 are rendered vague and indefinite by the use of the term "derived from". It is unclear what is meant by said term. Is some chemical modification or some other process involved in said derivation? As written it is impossible to determine the metes and bounds of the claimed invention.

Claim 9 is rendered vague and indefinite by the use of the phrase "sequence of interest". It is unclear what is meant by said term. What criteria is used to determine whether a given sequence is "of interest"? As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim 9 is rendered vague and indefinite by the use of the phrases "preferably 4 to 15 monomer units " and "more preferably 5 to 10 monomer units". It is unclear whether these are limitations of the claimed invention.

Claim 10 is rendered vague and indefinite by the use of the phrase "under the form". Is the claimed inhibitor to be covered by a MAP matrix or is MAP matrix a description of the chemical structure of the inhibitor? As written, it is impossible to determine the metes and bounds of the claimed invention.

Regarding claim 13, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

The instant invention is drawn to various fragments of nucleolin that function to inhibit interaction between gp120 of the HIV retroviruses and the V3 loop (nucleolin).

Claims 2-4, 6, 10 and 13 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Suzuki et al. (Biochemical Journal, Vol. 289 Part 1, pages 109-115, January 1, 1993).

Suzuki et al. disclose a method whereby they generated fragments of nucleolin. Said method included: cleavage of purified nucleolin by *N*-bromosuccinimde (NBS) or endogenous proteases; separation of fragments on SDS/PAGE; digestion of the resulting fragments (bands) with V8 protease (see pages 109-110).Since the entire nucleolin protein was digested, in absence of evidence to the contrary, the method of Suzuki et al. would generate all of the peptides/fragments of the claimed invention. While Suzuki et al. do not specifically describe using their peptide/fragments for the inhibition of gp120/nucleolin binding, it would be an inherent property of the fragment. Determination of the biological/chemical properties of each peptide/fragment would be obvious to one of skill in the art.

Claims 2-4, 6, 9-10 and 13 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Sapp et al. (European Journal of Biochemistry, Vol. 179 No. 3, pages 541-548, February 15, 1989).

Sapp et al. disclose a method whereby they generated fragments of nucleolin. Said method included the cleavage of purified nucleolin endogenous proteases and the sequencing of the resulting fragments (see page 542). Since the entire nucleolin protein was digested, in absence of evidence to the contrary, the method of Sapp et al. would generate all of the peptides/fragments of the claimed invention. While Sapp et al. do not specifically describe using their

peptide/fragments for the inhibition of gp120/nucleolin binding, it would be an inherent property of the fragment. Determination of the biological/chemical properties of each peptide/fragment would be obvious to one of skill in the art.

Claim Rejections - 35 USC § 103

Claims 2-6, 9-10 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Srivastava et al. (FEBS Letters, Vol. 250 No.1, pages 99-105, 1989).

Srivastava et al. disclose the complete nucleotide and amino acid sequence for human nucleolin (see page 101). Srivastava et al. further disclose a comparison between nucleolin from humans, chickens and hamsters. Since the entire nucleolin protein was incorporated in the cDNA library (see page 109), in absence of evidence to the contrary, said library would generate all of the peptides/fragments of the claimed invention. While Srivastava et al. do not specifically describe using their peptide/fragments for the inhibition of gp120/nucleolin binding, it would be an inherent property of the fragment. Determination of the biological/chemical properties of each peptide/fragment would be obvious to one of skill in the art. Additionally, since Srivastava et al. knew the sequences of the cDNA fragments (see page 109), it would have been obvious to one of skill in the art to modify said sequence so that the resulting peptide would have enhanced stability etc. One would have been motivated to make such modifications in order to protect said peptides from endogenous proteases thus increasing the half-life of said peptides.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure . Rankin et al., (Nucleic Acids Research, Vol. 21 No. 1, page 169) and Callebaut et al., (Journal of Biological Chemistry, Vol. 272 No. 11, 7159-7166, March 14, 1997) both describe nucleolin peptides/fragments. Additionally, Callebaut et al. disclose the use of said peptides to interfere with viral binding.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 308-7991. The examiner can be reached between the hours of 7:30 am and 4:00 pm Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, Donna Wortman, Primary Examiner can be reached at (703) 308-1032 or the examiner's supervisor, Lynette Smith, can be reached at (703)308-3909.

DONNA WORTMAN
PRIMARY EXAMINER

Robert A. Zeman

June 28, 2001